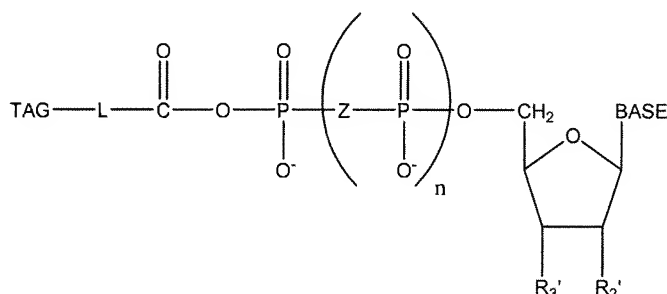


Amendments to the Claims/Listing of Claims

Please amend claims 1, 9 and 14-19, and add new claims 30-34 as follows. In addition, please cancel claims 22-26 without prejudice. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A tagged acyl phosphate or phosphonate probe according to claim 28 wherein X is a nucleotide, such that said probe has the formula:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), =O, acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, or -(CH₂)_mOH;

R₂' and R₃' are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH, or

-(CH₂)_m-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH;

n is 0-2;

m is 0 to 6; **[[and]]**

TAG **is as defined above,**

each Z is independently O, S, NH, or methylene; and

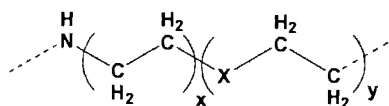
L **and each R** are as previously defined.

2. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is a purine.
3. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is a pyrimidine.
4. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, cytosine, inosine, 5-bromouracil, 5-fluorouracil, 2-aminopurine, N⁶-cyclohexyl adenine, 8-azaguanine, and 5-fluorocytosine.
5. (Previously presented) A tagged acyl-nucleotide probe according to claim 4, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, and cytosine.

6. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein R_2' and R_3' are independently H or OH.

7. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein R_2' and R_3' are each OH.

8. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein L has the structure:

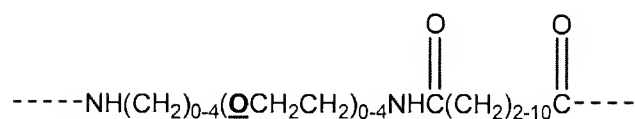
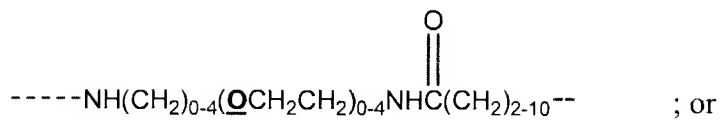
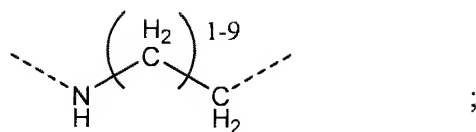


wherein

x and y are independently in the range of 0 to 4, and

X is O or CH_2 .

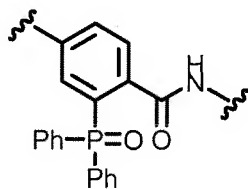
9. (Currently amended) A tagged acyl-nucleotide probe according to claim 1, wherein L has the structure:



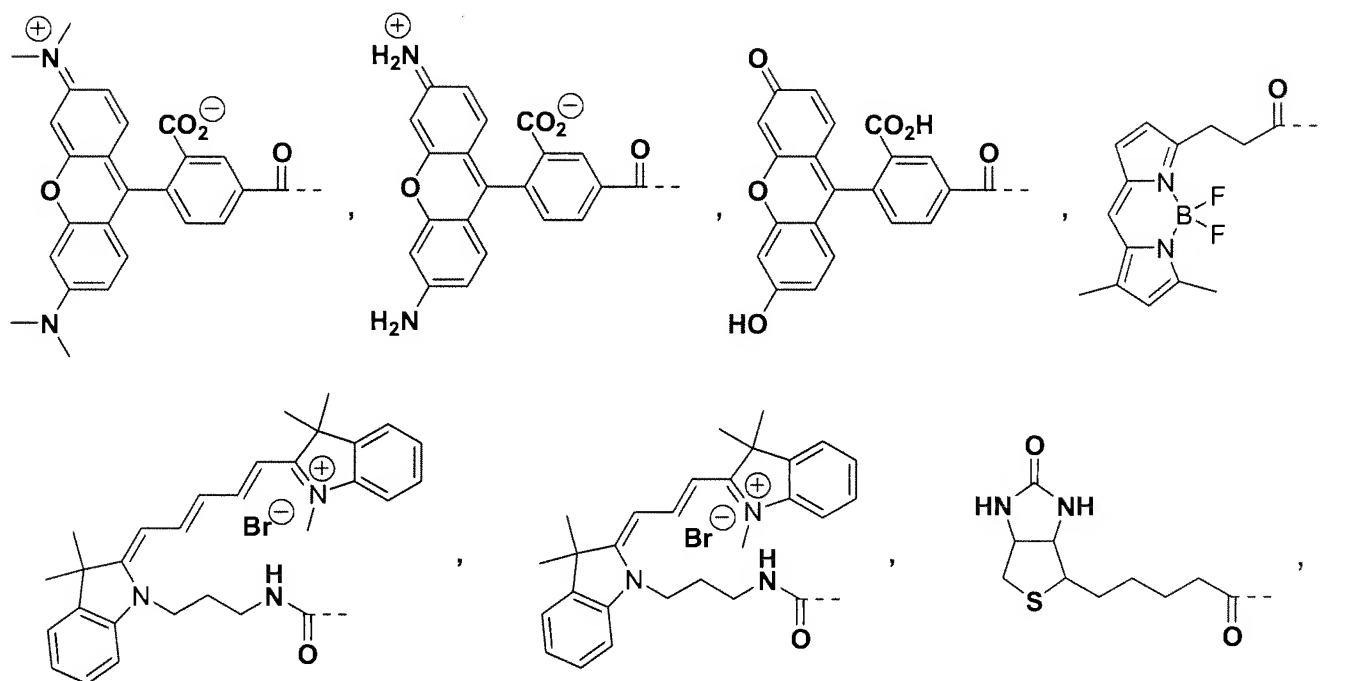
10. (Withdrawn) A tagged acyl-nucleotide probe according to claim 8, wherein L has the structure $\text{---NH}(\text{CH}_2)_2(\text{OCH}_2\text{CH}_2)_{1-4}\text{---}$.

11. (Withdrawn) A tagged acyl-nucleotide probe according to claim 1, wherein L comprises a triazole moiety.

12. (Withdrawn) A tagged acyl nucleotide probe according to claim 1, wherein L comprises the following moiety:

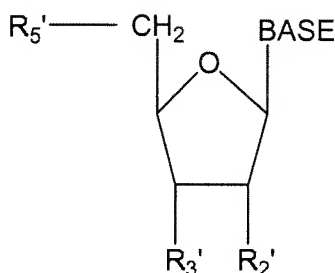


13. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein the TAG is selected from the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

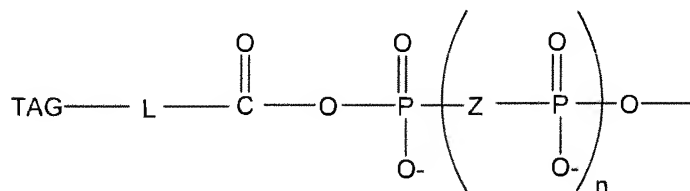
14. (Currently amended) A tagged acyl phosphate or phosphonate probe according to claim 28 wherein X is a nucleotide, such that said probe has the structure:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), =O, acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, or -(CH₂)_mOH;

one of R₂', and R₃', and R₅' has the following structure:



and the other two of R_2 , R_3 , and R_5 are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH, or -(CH₂)_m-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH;

n is 0-2;

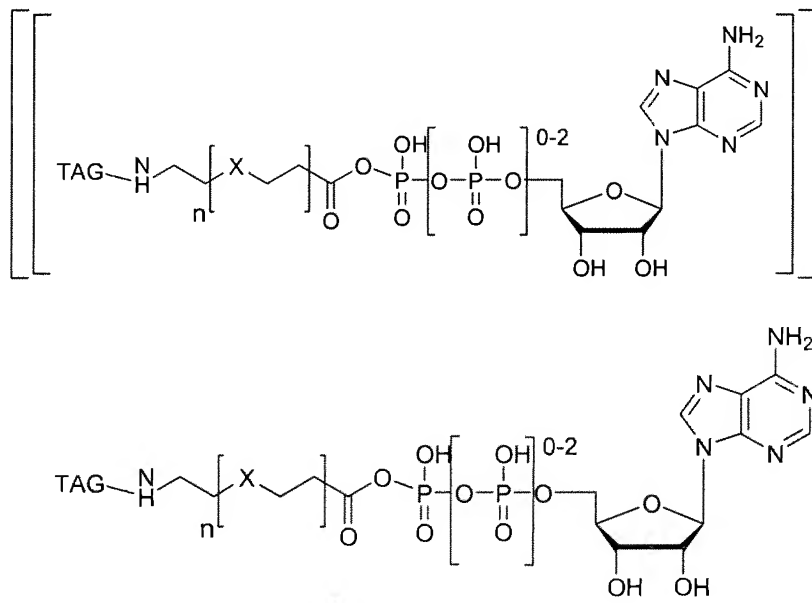
m is 0 to 6; **[[and]]**

TAG is as defined above,

each Z is independently O, S, NH, or methylene; and

L and each R are as previously defined.

15. (Currently amended) A tagged acyl-nucleotide probe having the structure:



wherein

n is 1-4;

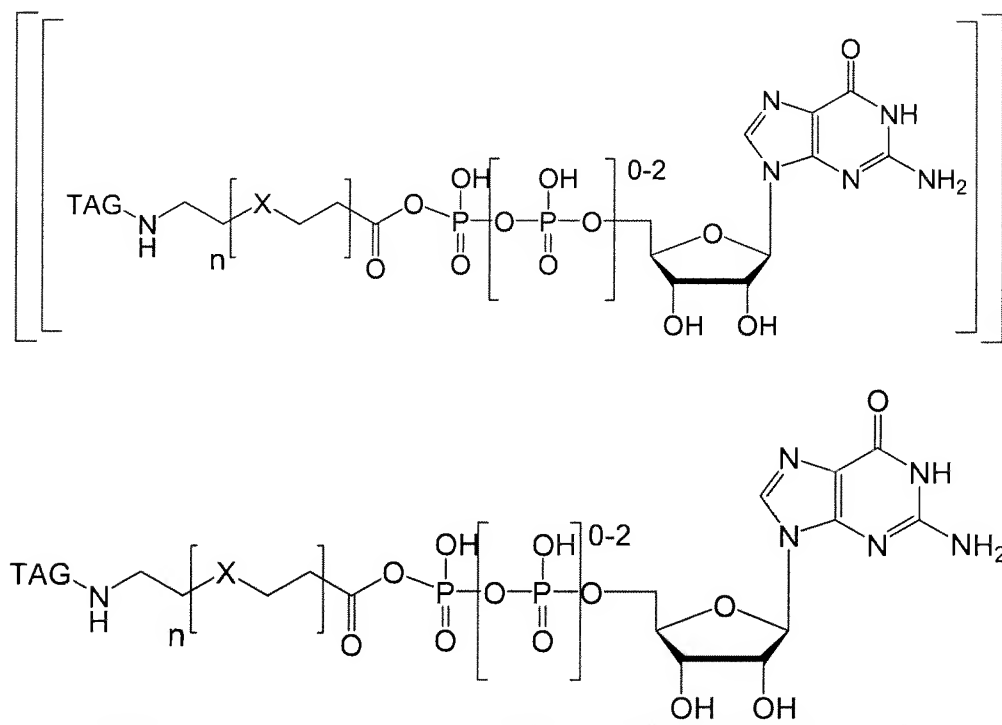
X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

16. (Currently amended) A tagged acyl-nucleotide probe having the structure:

wherein



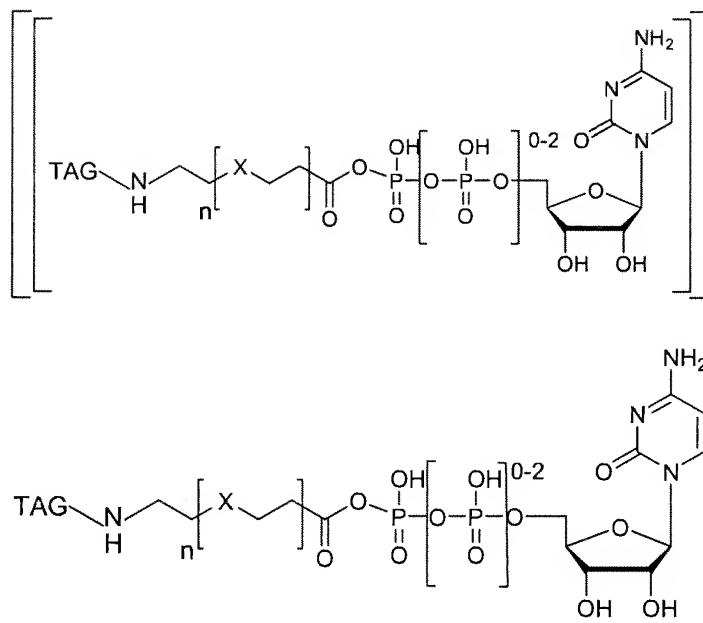
n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

17. (Currently amended) A tagged acyl-nucleotide probe having the structure:



wherein

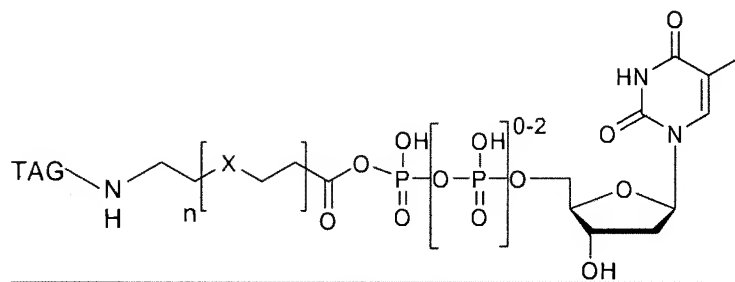
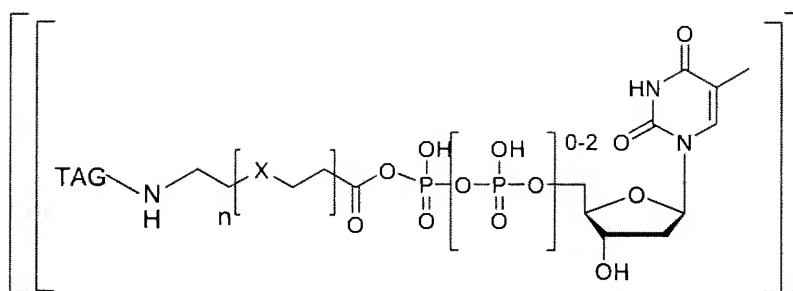
n is 1-4;

X is O or CH_2 ; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

18. (Currently amended) A tagged acyl-nucleotide probe having the structure:



wherein

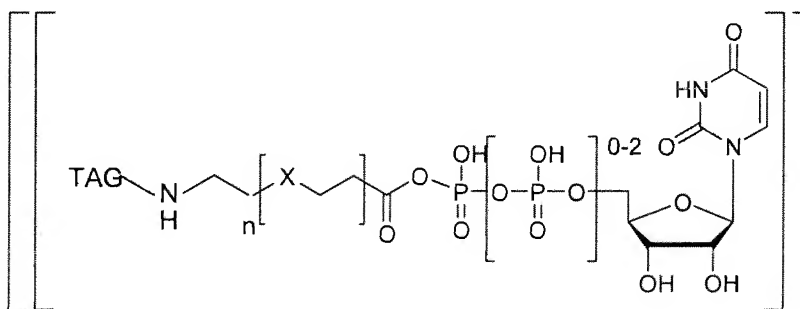
n is 1-4;

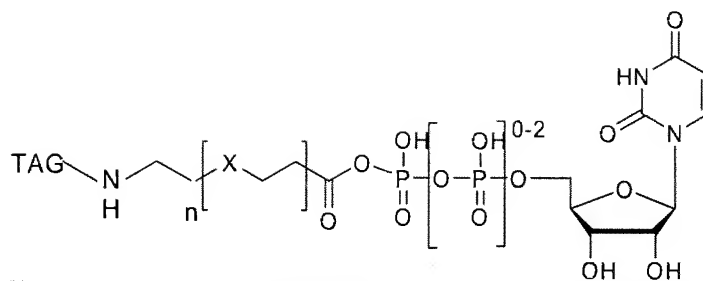
X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

19. (Currently amended) A tagged acyl-nucleotide probe having the structure:





wherein

n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

20. (Withdrawn) A method for determining the enzyme profile of one or more target proteins in a complex protein mixture, employing one or more probes comprising a nucleotide covalently bound through the terminal phosphate of a 5' mono- di- or tri-phosphate to an acyl group, which is further covalently bound to a TAG via a linker moiety "L", wherein said acyl group forms an adduct with said target protein(s) when said probe is bound to said target protein(s), said method comprising:

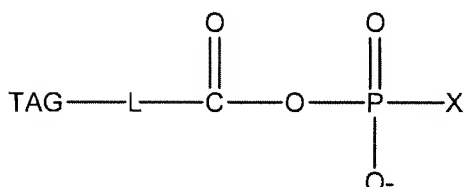
combining in a reaction medium said probe(s) and said complex protein mixture under conditions of reaction of said probe(s) with said nucleotide binding protein(s), whereby a conjugate of said probe(s) and said target protein(s) is formed; and determining said enzyme profile by generating a signal from one or more conjugates formed thereby;

wherein said probe(s) are selected from the nucleotide binding protein-directed probes of one of claims 1-18.

21. (Withdrawn) A method according to Claim 20, wherein said probe binds to a plurality of target proteins.

22. – 26. (Cancelled)

27. (Previously presented) A tagged acyl phosphate or phosphonate probe having the formula:



wherein

X is an affinity moiety for directing the binding of said TAPP to one or more target proteins linked to the phosphate through an oxygen or carbon;

TAG is a detectable label;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;

each R is independently H or -C₁₋₆ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and

the carbonyl adjacent to L is bound to a carbon to form an acyl group;

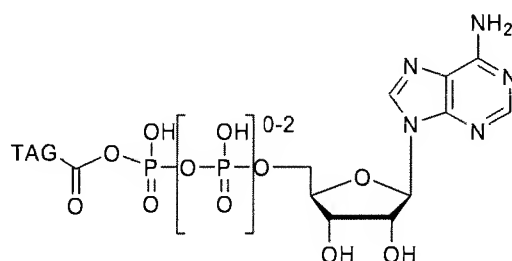
or a pharmaceutically acceptable salt or complex thereof.

28. (Original) The tagged acyl phosphate probe of claim 27, wherein X is selected from the group consisting of a nucleotide, nucleotide analogue, optionally substituted naphthyl group, small molecule, steroid, peptide hormone, enzyme cofactor, vitamin, enzyme substrate, lipid, prostaglandin, or receptor ligand.

29. (Withdrawn) A method of synthesizing a tagged acyl phosphate or phosphonate probe, comprising:

contacting a detectable label comprising a linking group L terminating in a carboxyl group, with a nucleotide or nucleotide analogue comprising a 5'-linked phosphate comprising an available -OH group in the presence of diisopropylcarbodiimide or isobutyl chloroformate and triethylamine to form said tagged acyl phosphate or phosphonate probe; and
purifying said probe.

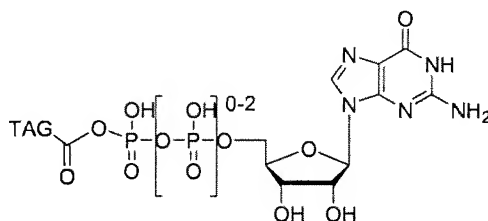
30. (New) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

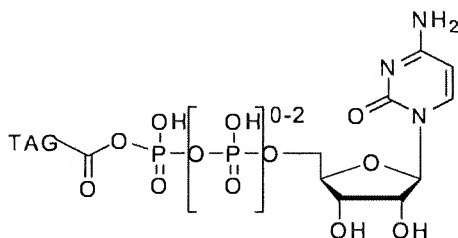
31. (New) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

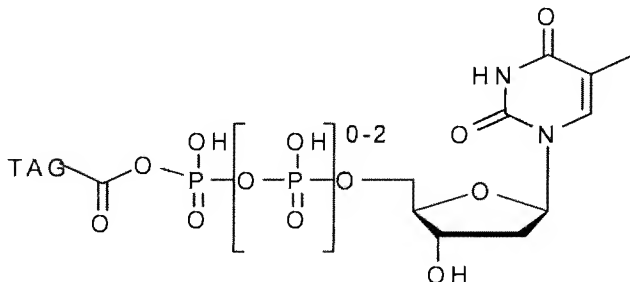
32. (New) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

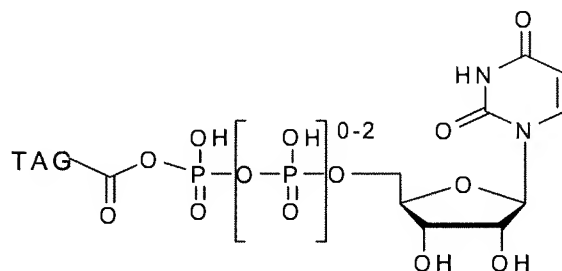
33. (New) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

34. (New) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.